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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/706,877	11/12/2003	Stuart L. Schreiber	42697.137 (US8)	5816
23483 7590 12/18/2006 WILMER CUTLER PICKERING HALE AND DORR LLP 60 STATE STREET BOSTON, MA 02109			EXAMINER RAMACHANDRAN, UMAMAHESWARI	
			ART UNIT	PAPER NUMBER
			1617	
SHORTENED STATUTORY PERIOD OF RESPONSE		MAIL DATE	DELIVERY MODE	
3 MONTHS		12/18/2006	PAPER	

**Please find below and/or attached an Office communication concerning this application or proceeding.**

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

<b>Office Action Summary</b>	Application No. 10/706,877	Applicant(s) SCHREIBER ET AL.	
	Examiner Umamaheswari Ramachandran	Art Unit 1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

#### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

- 1) ☒ Responsive to communication(s) filed on 26 October 2006.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

- 4) ☒ Claim(s) 1-11 is/are pending in the application.
- 4a) Of the above claim(s) 1 and 11 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 2-10 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

#### Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

#### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

#### Attachment(s)

- |   |   |
|---|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)  | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                                  | 5) <input type="checkbox"/> Notice of Informal Patent Application                       |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)<br>Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____  |

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**DETAILED ACTION**

Claims 1-11 are pending. Claims 1 and 11 are withdrawn as applicants had elected claims 2-10 are drawn to a method of treatment of cancer by various bicyclic heterocyclic compounds. Election was made with traverse in the reply filed on 10/26/2006 is acknowledged. The traversal is on the ground(s) that search of Group II will inevitably reveal art to the other group and that simultaneous search would not be unduly burdensome. This is not found persuasive as group I encompasses a broader claim (claim 1) and the different inventions use structurally distinct compounds for the treatment of cancer. The searches for group I and II may be overlapping but group I requires further additional search. Thus the restriction requirement elected is made final. The requirement is still deemed proper and is therefore made FINAL.

Claims 1 and 11 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on October 26 2006.

**Objection to Specification**

The specification (p 4, line 4) is objected for the following reasons: R<sup>3</sup> substitution "or deleted" is not clear. Appropriate correction is required.

***Claim Rejections - 35 USC § 112***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

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Claims 2-10 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for cell cycle analysis with lactacystin does not reasonably provide enablement for the treatment of all types of cancer. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to the invention commensurate in scope with these claims.

The instant specification fails to provide information that would allow the skilled artisan to practice the instant invention without undue experimentation. Attention is directed to *In re Wands*, 8 USPQ2d 1400 (CAFC 1988) at 1404 where the court set forth the eight factors to consider when assessing if a disclosure would have required undue experimentation. Citing *Ex parte Forman*, 230 USPQ 546 (BdApls 1986) at 547 the court recited eight factors:

(1) the nature of the invention; (2) the state of the prior art; (3) the relative skill of those in the art; (4) the predictability or unpredictability of the art; (5) the breadth of the claims; (6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary.

**(1) The nature of the Invention:**

The rejected claims are drawn to a method of treating cancer comprising administering a compound of formula listed in claim 2.

**(2) Breadth of the claims:**

Claims 2, 3 and 4 are broad as they drawn to a method of treating various types of cancer comprising administering a compound of formula listed in claim 2. The

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complex nature of the subject matter of this invention is greatly exacerbated by the breadth of the claims.

**(3) Guidance of the Specification:**

The guidance given by the specification for treating various types of cancer comprising administering a compound of formula listed in claim 2 is none. No examples are provided for treating various types of cancer comprising administering a compound of formula listed in claim 2. The only example provided is the cell cycle analysis with lactacystin and no examples are provided for any of the lactacystin analogs including the species elected.

The specification does not provide any relationship to how the cell cycle analysis could be useful for the treatment of cancer.

**(4) Working Examples:**

The specification does not provide any examples for treating various types of cancer comprising administering a compound of formula listed in claim 2. The only example provided is the cell cycle analysis with lactacystin and no examples are provided for any of the lactacystin analogs including the species elected.

**(5) The relative skill of those in the art:**

The relative skill of those in the medical treatment art is high, requiring advanced education and training.

**(6) The predictability of art:**

Claims 2, 3 and 4 are directed to a method of treating various types of cancer comprising administering a compound of formula listed in claim 2. The claims are so

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broad and there is a high degree of unpredictability involved. Despite the advanced training in the medical treatment arts, the arts are highly unpredictable.

**(7) The Quantity of Experimentation Necessary:**

In order to practice the above claimed invention, one of skill in the art would have to first envision formulation, dosage, duration, route and, in the case of human treatment, an appropriate animal model system to test the lactacystin analog compound of formula listed in claim 2, to determine whether or not they are useful in the treatment of every type of cancer listed in claim 4. If unsuccessful, which is likely given the lack of significant guidance from the specification or prior art regarding the treatment of various types of cancers by lactacystin analog compound of formula listed in claim 2, one of skill in the art would have to envision a modification in the formulation, dosage, duration, route of administration etc. and appropriate animal model system, or envision an entirely new combination of the above and test the system again. Therefore, it would require undue, unpredictable experimentation to practice the claimed invention of treating various types of cancers comprising administering a compound of formula listed in claim 2. Applicant fails to provide information sufficient to practice the claimed invention, absent undue experimentation. Genetech, 108 F.3d at 1366 states that "a patent is not a hunting license. It is not a reward for search, but compensation for its successful conclusion" and "patent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable".

***Claim Rejections - 35 USC § 112***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 2, 5-10 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for cell cycle analysis with lactacystin does not reasonably provide enablement for any other compound of formula listed in claim 2. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to the invention commensurate in scope with these claims.

The instant specification fails to provide information that would allow the skilled artisan to practice the instant invention without undue experimentation. Attention is directed to *In re Wands*, 8 USPQ2d 1400 (CAFC 1988) at 1404 where the court set forth the eight factors to consider when assessing if a disclosure would have required undue experimentation. Citing *Ex parte Forman*, 230 USPQ 546 (BdApls 1986) at 547 the court recited eight factors:

(1) the nature of the invention; (2) the state of the prior art; (3) the relative skill of those in the art; (4) the predictability or unpredictability of the art; (5) the breadth of the claims; (6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary.

**(1) The nature of the Invention:**

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The rejected claims are drawn to a method of treating cancer comprising administering a compound of formula listed in claim 2.

**(2) Breadth of the claims:**

Claim 2 is broad as it is drawn to a method of treating cancer comprising administering a compound of formula listed in claim 2. The complex nature of the subject matter of this invention is greatly exacerbated by the breadth of the claim.

**(3) Guidance of the Specification:**

The guidance given by the specification for treating cancer comprising administering a compound of formula listed in claim 2 is none. No examples are provided to treat cancer comprising administering a compound of formula listed in claim 2. The only example provided is the cell cycle analysis with lactacystin and no examples are provided for any of the lactacystin analogs including the species elected.

The specification does not provide any relationship to how the cell cycle analysis could be useful for the treatment of cancer.

**(4) Working Examples:**

The specification does not provide any examples for treating cancer comprising administering a compound of formula listed in claim 2. The only example provided is the cell cycle analysis with lactacystin and no examples are provided for any of the lactacystin analogs including the species elected.

**(5) The relative skill of those in the art:**

The relative skill of those in the medical treatment art is high, requiring advanced education and training.



**(6) The predictability of art:**

Claim 2 is directed to a method of treating cancer comprising administering a compound of formula listed in claim 2. The claim is so broad and there is a high degree of unpredictability involved. Despite the advanced training in the medical treatment arts, the arts are highly unpredictable.

**(7) The Quantity of Experimentation Necessary:**

In order to practice the above claimed invention, one of skill in the art would have to first envision formulation, dosage, duration, route and, in the case of human treatment, an appropriate animal model system to test every lactacystin analog compound of formula listed in claim 2, to determine whether or not they are useful in the treatment of cancer. If unsuccessful, which is likely given the lack of significant guidance from the specification or prior art regarding the treatment of cancer by lactacystin analog compounds of formula listed in claim 2, one of skill in the art would have to envision a modification in the formulation, dosage, duration, route of administration etc. and appropriate animal model system, or envision an entirely new combination of the above and test the system again. Therefore, it would require undue, unpredictable experimentation to practice the claimed invention of treating cancer comprising administering the compounds of formula listed in claim 2. Applicant fails to provide information sufficient to practice the claimed invention, absent undue experimentation. Genetech, 108 F.3d at 1366 states that "a patent is not a hunting license. It is not a reward for search, but compensation for its successful conclusion" and "patent

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protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable”.

***Claim Rejections - 35 USC § 112***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 2 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 2, p4, and lines 17-18 indicate the R<sup>3</sup> substitution as “or deleted” which is not clear. Appropriate correction is required.

***Claim Rejections - 35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 2-5, 9 and 10 are rejected under 35 U.S.C. 102(a) as being anticipated by Fenteany et al (PNAS, Vol. 91, pp 3358-3362).

Fenteany et al. teaches clasto lactacystin  $\beta$ -lactone (elected species of claim 2) inhibits cell cycle progression in an osteosarcoma cell line (Abstract, p3359, col. 2 para 2, p 3361, Table 2, compound 4). The reference teaches that the existence of a lactacystin target in cells is implied by the inhibition of MG-63 osteosarcoma cells by lactacystin and lactacystin analogs from progressing beyond the G<sub>1</sub> phase of the cell cycle (p 3361, col. 2, para 1, lines 4-6, p 3359, col. 2, para 2). The reference inherently teaches the treatment of osteosarcoma by inhibiting the cell cycle progression.

**Conclusion**

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Umamaheswari Ramachandran whose telephone number is 571-272-9926. The examiner can normally be reached on M-F 8:30 AM - 5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan can be reached on 571-272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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